**518-Pos Board B273**
**Role of M2 Influenza Protein on Viral Budding and Scission**
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M2 is a pH-dependent matrix protein from influenza virus widely known for its role in viral uncoating and the target of the amantadine flu drug that prevents proton transport. An additional role played by M2 relies on collective effects where clusters of M2-homotetramer proteins have been hypothesized to induce local membrane curvature effects (Rossman et al., Cell 142, pp. 902-913, 2010).
We use molecular dynamics simulations with the MARTINI coarse grained parametrization to study a system comprised by two model membranes linked by an hour-glass shaped structure. We study the role played by M2 homotetramers in the scission step, leading to lipid-bilayer separation. The geometry of the model and the membrane-lipid interaction details are further used to adjust parameters on a Helfrich-like functional in order to propose a minimal model for viral scission at the mesoscopic scale.

**519-Pos Board B274**
**Comparative Analysis of Inorganic Phosphate Binding in a Synthetic and a Native P-Loop Peptide Using Molecular Dynamics Simulations**
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Binding of anions by proteins is a topic of great interest, the binding being due to interactions either with the protein's positively charged side chains and/or with the main chain. In particular the phosphate anion is essential for a large number of functions and pathways within cells, and the specific binding of phosphate anion has been widely studied. However, investigation of the structural features in phosphate binding sites and the mechanisms for phosphate binding is still a field that warrants more research.
One of the most common ways in which proteins bind to phosphate is via a highly conserved consensus sequence that folds into what is known as a P-loop. Here, we use molecular mechanics and quantum mechanical calculations to characterize interactions of the phosphate anion with 1) a native P-loop whose structure available in the PDB database (1MAB), and 2) a synthetic peptide designed to bind phosphate by mimicking the P-loop function. Whereas the structure of the native P-loop is fairly well characterized and restricted within the 1MAB structure, the synthetic peptide explores a larger conformational space - yet the synthetic peptide is able to bind phosphate.
Specifically we investigate the structural properties and the conformational space of both the peptides, we characterize how they interact with phosphate, and we examine the mechanism by which the peptides fold into the P-loop structure and bind phosphate.

**520-Pos Board B275**
**Computational Study of Transmembrane Helix-Helix Interactions in Model Peptides Derived from the DesK Minimal Sensor**
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DesK is a bacterial transmembrane protein that acts as a molecular switch to regulate membrane fluidity as a function of temperature change. The full function of DesK has been experimentally modeled by a chimeric construct, denominated minimal sensor (MS), consisting of a single transmembrane (TM) helix. Multiple mutants based on the TM part of DesK-MS have been reported, suggesting that DesK is sensitive to changes in membrane thickness as a result of changes in temperature. The current view of DesK-MS signaling mechanism points towards formation of a dimer capable of switching its conformation depending on the temperature.
In this study we investigate the molecular details of the functioning of the DesK-MS using experimentally developed model peptides of the TM part only, both the wild type and some of its mutants. We employ a method recently developed in our group for exploring the energy landscape of helix-helix interactions in the membrane environment, which allows high throughput screening of trans-membrane helix dimers. In order to gain more insight into the interactions between the dimers and their lipid environment, a multiscale approach is used. The results presented here are compared to the available experimental data and provide basis for further exploration of the molecular basis of the switch mechanism in DesK-MS.

**521-Pos Board B276**
**Charged Protein-Lipid Interactions in Bilayers with Wide-Ranging Thickness**
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Charged amino acids play important roles in membrane protein structure and function. All-atom molecular dynamics (MD) studies have previously been applied to investigate the mechanisms by which charged groups move through lipid bilayers, but have not fully explored the wide range of membrane topologies that may influence charge transport. Here we have performed simulations of the arginine (Arg) side chain analog, $MguanH^+$, moving across bilayers of mono-unsaturated phosphatidylcholine (PC) with 14-24 carbon tails, with and without cholesterol (in a 2:1 lipid:cholesterol ratio), generating hydrophobic thickness increasing systematically from 24 to 42 Angstrom. We demonstrate that free energies grow in proportion to membrane thickness due to an ion-induced defect mechanism, where the presence of the ion leads to membrane deformations and sharp free energy barriers ranging from 14 kcal/mol in D14:1PC to 40 kcal/mol in D24:1PC+cholesterol. Our findings provide a deeper understanding of membrane charge transport phenomena, including uncatalyzed ion permeation and the actions of membrane-active charged peptides for a range of membrane compositions.

**522-Pos Board B277**
**Capturing Spontaneous Binding of Human Islet Amyloid Polypeptide to Anionic Membranes using a Highly Mobile Membrane Mimetic Model**
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Human islet amyloid polypeptide (hIAPP) aggregates and forms amyloid fibrils in the pancreas of patients with type2 diabetes. Anionic membranes bind hIAPP and accelerate the fibril formation. During this process, hIAPP disrupts the membrane, a toxic process that has been associated with the N-terminal 19 residues and proposed to lead to the destruction of the insulin-producing β-cells in the pancreas. The mechanism by which the membrane is disrupted is therefore key to our understanding of toxicity of hIAPP, and to design of effective disease modifying treatments.
Employing molecular dynamics (MD) simulations, we have investigated the molecular events key to hIAPP binding to anionic phospholipid bilayers. The diffusion of lipids in conventional membrane models is too slow to allow for hIAPP-membrane binding on the time-scale feasible with conventional MD simulations. In order to overcome the slow diffusion of lipids in conventional membranes which might not allow for adequate sampling of the binding of hIAPP binding to the membrane, we have employed a highly mobile membrane mimetic (HMMM) model.
Multiple independent MD simulations, amounting to 1.2 μs, both for the N-terminal 19-residue peptide, and for the full (37-residue) hIAPP, resulted in spontaneous binding to mixed anionic/zwitterionic HMMM membranes. Initial contacts between the peptide and lipids, which form rapidly (within the first 10 ns of the simulations), are mediated by a group of positively charged residues, Lys1, Arg11, and His18, indicating that the N-terminal part of hIAPP is responsible for its interaction with anionic membranes. These simulations have provided an unprecedented level of statistic on lipid-protein interaction for hIAPP peptides, characterizing residues and lipid chemical groups key for bindig and interaction, as well as the structure and dynamics of the peptide in its membrane-bound form.

**523-Pos Board B278**
**Molecular Dynamics Studies of PEGylated Antimicrobial Peptides with Lipid Bilayers**
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We performed all-atom molecular dynamics (MD) simulations of polyethylene glycol (PEG)-grafted magainin 2 and tachyplesin I with lipid bilayers. In the simulations of PEGylated magainin 2 and tachyplesin I in water, both peptides are wrapped by PEG chains because of the interaction between oxygens of PEGs and the cationic residues of peptides. The α-helical structure of PEGylated magainin 2 is broken, while β-sheet of PEGylated tachyplesin I keeps stable, similar to the structural behavior of unPEGylated peptides, in agreement with experiments. Simulations of PEGylated peptides with lipid bilayers show that PEG chains block the electrostatic interaction between cationic residues of peptides and anionic phosphates of lipids, leading to the less binding of the peptide to the bilayer surface, which is observed more significantly for magainin 2 than